Written evidence from Dr Joshua Biggs O'May (ENB0032)

Here I present evidence on CRISPR gene editing, a key area of strength for the UK engineering biology sector, with further potential for investment, innovation, and both clinical and commercial application.

The development of CRISPR gene editing technology is recognised as one of the biggest breakthroughs in life science research this century. The market for CRISPR technologies is expected to reach $17.8bn by 2034 from $3.4bn today[1]. The UK government has been heavily involved in the development of CRISPR therapeutics through funding primary research and clinical trials[2]. It is also leading the field in CRISPR policy by being the first to license a CRISPR-based therapy of any kind, known as Casgevy[3].

Thus far, CRISPR therapeutics have been designed to cut and paste sections of DNA sequence. However, the same CRISPR system can be used to edit DNA in other ways. One particularly promising application is epigenetic editing. In this context, rather than cutting the DNA, the CRISPR technology changes the way that the DNA sequence is 'read', thereby tuning gene activity[4–6]. This approach has huge potential to treat many classes of disease and avoids some of the main risks associated with the earlier CRISPR therapies. Furthermore, the new generation of CRISPR therapeutics will benefit greatly from any ongoing research addressing the problems encountered by the first wave of CRISPR therapeutics, such as off-target effects[7]. Therefore, the new therapies could enjoy an accelerated journey to the clinic.

Already several companies developing these treatments have been established in the US and Japan, with one clinical trial now underway[8–10]. The UK government should consider how to accelerate UK-based innovation in this field by leveraging existing expertise, infrastructure, and capacity for innovation. It could:

- increase funding for epigenetics research.
- facilitate and fund the UK arm of international clinical trials, as it did with Casgevy.
- help UK institutions translate research and sponsor clinical trials, just as the Great Ormond Street Hospital has done with earlier CRISPR technologies[11,12].

The UK could also capitalise on its position as a world leader in CRISPR policy by bringing together policymakers, the international research community, and people with lived experience to develop guidance and regulation for these new therapies[13–15].

07 May 2024

References

(1) **CRISPR Market to Explode: $3.4 Billion Today, $17.8 Billion by 2034, Fueled by Investment Surge** | Future Market Insights, Inc. MarketWatch. https://www.marketwatch.com/press-release/crispr-market-to-explode-3-4-billion-today-17-8-billion-by-2034-fueled-by-investment-surge-future-market-insights-inc-5ddebc55.

(2) **UK medicines regulator approves world-first gene-editing treatment for blood disorders**. https://www.imperial.nhs.uk/about-us/news/uk-medicines-regulator-approves-world-first-gene-editing-treatment-for-blood-disorders.

(3) **UK approves world-first gene-editing treatment for blood disorders** | Imperial News | Imperial College London. Imperial News. https://www.imperial.ac.uk/news/249536/uk-approves-world-first-gene-editing-treatment-blood/.

(4) Ledford, H. **CRISPR 2.0: A New Wave of Gene Editors Heads for Clinical Trials**. Nature 2023, 624 (7991), 234–235. https://doi.org/10.1038/d41586-023-03797-7.

(5) Saunderson, E. A.; Encabo, H. H.; Devis, J.; Rouault-Pierre, K.; Piganeau, M.; Bell, C. G.; Gribben, J. G.; Bonnet, D.; Ficz, G. **CRISPR/dCas9 DNA Methylation Editing Is Heritable during Human Hematopoiesis and Shapes Immune Progeny**. Proceedings of the National Academy of Sciences 2023, 120 (34), e2300224120. https://doi.org/10.1073/pnas.2300224120.

(6) Cappelluti, M. A.; Mollica Poeta, V.; Valsoni, S.; Quarato, P.; Merlin, S.; Merelli, I.; Lombardo, A. **Durable and Efficient Gene Silencing in Vivo by Hit-and-Run Epigenome Editing**. Nature 2024, 1–8. https://doi.org/10.1038/s41586-024-07087-8.

(7) Guo, C.; Ma, X.; Gao, F.; Guo, Y. **Off-Target Effects in CRISPR/Cas9 Gene Editing**. Front Bioeng Biotechnol 2023, 11, 1143157. https://doi.org/10.3389/fbioe.2023.1143157.

(8) Vuksanaj, K. **Epigenome Editing Companies Mark Preclinical Progress**. GEN - Genetic Engineering and Biotechnology News. https://www.genengnews.com/topics/genome-editing/epigenome-editing-companies-mark-preclinical-progress/.

(9) **Omega Therapeutics Announces Promising Preliminary Clinical Data for OTX-2002 from Ongoing MYCHELANGELO™** I Trial. BioSpace. https://www.biospace.com/article/omega-therapeutics-announces-promising-preliminary-clinical-data-for-otx-2002-from-ongoing-mychelangelo-i-trial/.

(10) Omega Therapeutics. **Phase 1/2 Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Preliminary Antitumor Activity of OTX-2002 as a Single Agent and in Combination With Standard of Care in Patients With Hepatocellular Carcinoma and Other Solid Tumor Types Known for Association With the MYC Oncogene**; Clinical trial

registration NCT05497453; clinicaltrials.gov, 2023. https://clinicaltrials.gov/study/NCT05497453.
(11) Great Ormond Street Hospital for Children NHS Foundation Trust. **Phase 1, Open Label Study of CRISPR-CAR Genome Edited T Cells (PBLTT52CAR19) in Relapsed /Refractory B Cell Acute Lymphoblastic Leukaemia**; Clinical trial registration NCT04557436; clinicaltrials.gov, 2024. https://clinicaltrials.gov/study/NCT04557436.
(12) Great Ormond Street Hospital for Children NHS Foundation Trust**. Phase 1 Study of Base Edited CAR7 T Cells to Treat T Cell Malignancies (TvT CAR7)**; Clinical trial registration NCT05397184; clinicaltrials.gov, 2023. https://clinicaltrials.gov/study/NCT05397184.
(13) **ORION Genome Editing Workshop and Public Dialogue** » Babraham Institute. https://www.babraham.ac.uk/events-galleries/orion.
(14) **2023 Human Genome Editing Summit** | Royal Society. https://royalsociety.org/science-events-and-lectures/2023/03/2023-human-genome-editing-summit/.
(15) **Cut + Paste Nights** | closing event. Crick. https://www.crick.ac.uk/whats-on/cut-paste-nights-closing-event.